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TITLE: Phase II Clinical Trial of Intraoral Grafting of Human Tissue-Engineered Oral Mucosa

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14. ABSTRACT

This is a randomized, parallel-group phase II study to assess the safety and efficacy for use of human EVPOME for soft tissue intraoral grafting procedures compared to the “gold standard” palatal oral mucosa (POM) graft. The study will determine differences in the primary efficacy measure of increased keratinized mucosa; secondary measures of graft contracture and Wound Healing Index; and ancillary outcome measures of tissue perfusion measured graft color and laser Doppler flowmetry, and postoperative pain. Sixty subjects, thirty subjects per treatment group, will be randomized to receive either the experimental treatment, EVPOME (Group 1), or standard of care, the palatal oral mucosa (POM) graft (Group 2). The study population will include non-smoking adults (ages 18 and older) in need of additional keratinized oral mucosa This trial has recently been awarded a No Cost Extention to continue it’s recruitment efforts.

15. SUBJECT TERMS

EVOPME, Palatal Oral Mucosa (POM), Keratinized mucosa, graft contracture

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Introduction

Reconstructive procedures of the oral cavity secondary to trauma fail to achieve a satisfactory aesthetic and functional outcome. A daunting challenge for reconstructive surgeons is to regenerate oral mucosa. The free mucosal graft neither reliably restores aesthetic and functional competence, nor prevents microbial infection, fluid loss, and foreign material contamination and relapse secondary to wound contracture. Oral mucosa is in limited supply for use in reconstructive procedures in the oral cavity. This is especially prevalent after large avulsed soft tissue wounds involving the mouth and lips seen in high velocity battlefield injuries (BI). The development of an oral mucosa equivalent is necessary to fulfill this clinical need. The environment of the oral cavity, a moist area laden with bacteria and lytic enzymes, is not favorable to most of the collagen-rich dermal components used in similarly designed skin equivalents. To be useful within the intricate confines of the oral cavity an oral mucosa equivalent must possess mechanical and handling characteristics as well as similar anatomy. Engineering an Ex Vivo Produced Oral Mucosa Equivalent (EVPOME) tissue will allow the reconstruction of major oral avulsion defects. These defects are seen as secondary to traumatic injuries or oncologic resection and developmental disturbances. The EVPOME will minimize patient morbidity and improve functional outcome measures. Consequently, the goal of our clinical trial is to determine efficacy of an EVPOME as a more robust therapy than palatal oral mucosa (POM) grafts.

Body

The Statement of Work for this project included the following:

1. Obtain IRB approval for study at University of Michigan-This has been obtained (HUM00065554).

2. Obtain IND approval from the FDA-This has been obtained (IND#: 10118).

3. Obtain approval of IRB from DoD-HRPO approval has been obtained.

4. Calibration of clinical examiners-There will only be one clinical examiner in this study so no calibration with other examiners will be necessary.

5. Calibration of laser Doppler flowmetry-This has been completed.

6. Initiation of subject screening/recruitment-Screening/recruitment is ongoing.

7. Construction and certification of a new cGMP facility; Clinical Tissue Manufacturing Laboratory (CTML): This has been completed.

8. Subjects are recruited through the clinics in the U-M School of Dentistry. The currently approved flyer and letter to clinicians are emailed to local dental offices. The flyers are approved for posting in these clinics. The study is also actively recruiting subjects on the UMHealthResearch.org website portal and the study is also posted on the Clinicaltrials.gov website.

9. Iwonka Eagle joined the team replacing Sarah Wesley as study coordinator. This change was approved by the IRB on 11/16/2016 and screening was started in January 2017.

10. Completion of subject screening/recruitment

Total Number of subjects consented (Visit 1)	**28**	
Total Screen failures at visit 1	11	
Withdrawal prior to randomization	3	
	POM Control Group	EVPOME
Completed study	5	2
In follow-up	1	0
Subject withdraw	1	3
Randomized	7	7
Pending surgery	0	2
Pending randomization	0	
Pending screening		

11. Inclusion of first subject into clinical trial. - At the time of this report 14 subjects have been enrolled in the control arm and 14 in the experimental arm.

12. Completion of clinical trial- This has not yet occurred.

13. Data evaluation from clinical trial – This has not yet occurred.

14. Submission of findings to meeting and peer reviewed journals -This has not yet occurred.

Key Research Accomplishments

Seven subjects have successfully completed the study. On October 14, 2015, the "Clinical Tissue Manufacturing Laboratory" (CTML) manufacturing team starting producing the EVPOME investigational product for the first experimental arm subject in the small defect study. A protocol amendment in early 2017revised the study inclusionary criteria to include all non-smoking subjects (ages 18 and older) in need of additional keratinized oral mucosa and provided recruitment materials to local dentists. This resulted in an increase in screening and enrollment numbers over the past year.

Reportable Outcomes

There are no reportable outcomes at this time.

Conclusion

The study team plans to continue aggressively screening subjects and hopes to maintain a consistent subject randomization to meet enrollment as soon as possible.